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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/165,460
Filing Date: October 02, 1998
Appellant(s): RINE ET AL.

Richard Aron Osman
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 1/13/2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The brief contains a statement indicating that Appellants are unaware of any related appeals or interferences.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is substantially correct. It is noted however that it is the polynucleotide of SEQ ID NO: 3 which encodes the product of the gene RCE1 and not the polynucleotide of SEQ ID NO: 2 as asserted in page 2 of the Brief.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The brief contains a statement indicating that the claims in each of the issues shall stand together as a group.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Rose et al., GenBank accession number Z49617, October 6, 1995.

Lye et al., GenBank accession number Z49260, May 16, 1995.

4,997,767 NOZAKI 3-1991

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 31 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rose et al. (GenBank accession number Z49617, October 6, 1995) in view of Nozaki et al. (U.S. Patent No. 4,997,767, March 1991). Rose et al. teaches a polynucleotide of 1825 nucleotides (locus SCYJR117W) which is identical to that of the polynucleotide of SEQ ID NO: 1 (1825 nucleotides) except for one mismatch at position 1664. See attached alignment provided for visualization purposes. The polynucleotide of Rose et al. would be expected to hybridize to the polynucleotide of SEQ ID NO: 1 under highly stringent conditions. Rose et al. does not teach an expression vector comprising said polynucleotide or a host cell transformed with an expression vector. Nozaki et al. teaches a yeast shuttle vector which comprises the repressible acid phosphatase promoter (column 1, lines 4-10) for expressing proteins in yeast which can replicate in *E. coli* and yeast. Nozaki et al. also teaches the transformation of yeast cells with such vector (column 7, line 50- column 8, line 27). Nozaki et al. does not teach a vector or a host cell comprising a polynucleotide which can hybridize under highly stringent conditions to the polynucleotide of SEQ ID NO: 1.

Claim 31 is directed to an expression vector comprising a polynucleotide operably linked to a promoter, wherein said polynucleotide hybridizes under highly stringent conditions to the polynucleotide of SEQ ID NO: 1 and wherein said polynucleotide encodes a polypeptide which mediates the proteolytic removal of an AAX tripeptide from a prenylated CAAX protein. Claim 39 is directed to a cell transformed with the vector of claim 31.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an expression vector, as taught by Nozaki et al., with the polynucleotide of Rose et al. and transform a host cell for the benefit of recombinantly producing sufficient amounts of the corresponding protein for functional characterization and determination of its biological role. A person of ordinary skill in the art is highly motivated to characterize and determine the biological role of a yeast (*S. cerevisiae*) protein since yeast is a unicellular eukaryote widely studied in the art for identification of proteins and/or biological processes which may be found in higher eukaryotes including humans. One of ordinary skill in the art has a reasonable expectation of success at making an expression vector with the polynucleotide of Rose et al. and transforming a host cell with such vector since Nozaki et al. teaches an expression vector which can be used in *E. coli* and yeast as well as the transformation of host cells with such vector. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Claims 35, 37-38, 43, 45 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lye et al. (GenBank accession number Z49260, May 16, 1995) in view of Nozaki et al. (U.S. Patent No. 4,997,767, March 1991). Lye et al. teaches a polynucleotide of (locus SC8156) which comprises the polynucleotide of SEQ ID NO: 3 in its entirety. See attached alignment provided for visualization purposes. The polynucleotide of Lye et al. would be expected to hybridize to the polynucleotide of SEQ ID NO: 3 under highly stringent conditions. Lye et al. does not teach an expression vector comprising said polynucleotide or a host cell transformed with an expression vector. Nozaki et al. teaches a yeast shuttle vector which comprises the repressible acid phosphatase promoter (column 1, lines 4-10) for expressing proteins in yeast which can replicate in *E. coli* and yeast. Nozaki et al. also teaches the transformation of yeast cells with such vector (column 7, line 50- column 8, line 27). Nozaki et al. does

not teach a vector or a host cell comprising a polynucleotide which can hybridize under highly stringent conditions to the polynucleotide of SEQ ID NO: 3.

Claim 35 is directed to an expression vector comprising a polynucleotide operably linked to a promoter, wherein said polynucleotide hybridizes under highly stringent conditions to the polynucleotide of SEQ ID NO: 3 and wherein said polynucleotide encodes a polypeptide which mediates the proteolytic removal of an AAX tripeptide from a prenylated CAAX protein. Claims 37 and 38 are directed to the expression vector of claim 35 wherein the polypeptide either comprises or consists of the polypeptide of SEQ ID NO: 4. Claims 43, 45 and 46 are drawn to host cells transformed with the vectors of claims 35, 37 and 38, respectively.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an expression vector, as taught by Nozaki et al., with the polynucleotide of Lye et al. and transform a host cell for the benefit of recombinantly producing sufficient amounts of the corresponding protein for functional characterization and determination of its biological role. A person of ordinary skill in the art is highly motivated to characterize and determine the biological role of a yeast (*S. cerevisiae*) protein since yeast is a unicellular eukaryote widely studied in the art for identification of proteins and/or biological processes which may be found in higher eukaryotes including humans. One of ordinary skill in the art has a reasonable expectation of success at making an expression vector with the polynucleotide of Lye et al. and transforming a host cell with such vector since Nozaki et al. teaches an expression vector which can be used in *E. coli* and yeast as well as the transformation of host cells with such vector. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

(11) Response to Argument

Issue I: Claims 31 and 39 are patentable under 35 USC 103(a)

In page 3, first paragraph, Appellants argue that Rose et al. is dated August 11, 1997, which is more than a year after Appellant's priority date. As such, Appellants submit the instant reference is not prior art. Appellants also submit that the Examiner now identifies additional supportive publications, in particular Swiss Prot accession number P47154. According to Appellants, while the date given in the first DT line of the Swiss Prot entry (February 1, 1996) is the date when the entry was first available for public disclosure, this entry also contains references to publications from 1997, 1998 and 2000, as well as reference to post-filing publications by Appellants. Therefore, Appellants submit that absent a time machine, it is impossible for an entry available in 1996 to make reference to publications in 2000.

Appellants appear to be confused as to why Swiss Prot accession number P47154 was introduced by the Examiner in the Examiner's Answer of 5/20/2003. The Examiner did not introduce the Swiss Prot entry as an additional supportive publication for the instant rejection. Swiss Prot accession number P47154 is the corresponding entry for the protein encoded by the polynucleotide disclosed in GenBank's entry Z49617, which was first disclosed on October 6, 1995. The Examiner did not and is not relying on Swiss Prot accession number P47154 as supportive evidence for the instant rejection as asserted by Appellants. Instead, the Examiner, as clearly indicated in the Examiner's Answer of 5/20/2003 (page 2, Issues) and the Final Action of 12/29/2003 (page 3, item 2), used the Swiss Prot entry to inform Appellants why the Examiner was withdrawing the rejection of claims 33-34 and 41-42. As stated in the Issues section of the Examiner's Answer of 5/20/2003, the polynucleotide of SEQ ID NO: 1 is identical to the polynucleotide of Rose et al. except for one mismatch at position 1664. Alignments were provided with the Examiner's Answer of 5/20/2003 for visualization purposes. The protein encoded by the polynucleotide of Rose et al. (Swiss Prot accession number P47154, February 1, 1996) is identical to the polypeptide of SEQ ID NO: 2 except for one mismatch at position 441. Since Rose et al. does not teach a polynucleotide which encodes the polypeptide of SEQ ID NO: 2 in its entirety, the teachings of Rose et

al. do not anticipate or make obvious the expression vector and host cells of claims 33-34 and 41-42, therefore the 35 USC 103(a) rejection of claims 33-34 and 41-42 was withdrawn.

In regard to the polynucleotide of GenBank accession No. Z49617, it is reiterated herein that the polynucleotide of GenBank accession No. Z49617 was first disclosed to the public on October 6, 1995 and not August 11, 1997, as asserted by Appellants. The creation date of the entry is the date when it is first available to the public, which in this case is October 6, 1995. While it is known in the art that the creation date corresponds to the date when a submission is first disclosed to the public, the PTO Biotechnology and Chemical Library contacted EMBL to specifically determine the date of public availability of entry Z49617. Appellants were informed in the Advisory Action of 2/21/2003 of such communication (page 2, item 3) and a copy of the e-mail communication with a representative of EMBL was submitted in the Examiner's Answer of 5/20/2003 to complete the record. Z49617 was first submitted to the EMBL databank. As it can be seen in such e-mail, it is clearly stated that the date given in the first DT line of the entry is the date the entry first became available for public disclosure. Therefore, for entry Z49617, that date corresponds to October 6, 1995, as shown in the e-mail. In the absence of any evidence which would suggest that the sequence in the instant entry was modified in 1997 or that there was a request to withhold its public disclosure until 1997, the Examiner must assume that the instant entry was first disclosed to the public on October 6, 1995.

Appellants have presented no evidence which would suggest that the polynucleotide disclosed by Rose et al. was withheld from public disclosure after its creation date or that it was updated or amended to the extent that its sequence is different from what it was when it was created in October 6, 1995. The Examiner acknowledges that entry Z49617 was updated in August 11, 1997. However there is no evidence in the record as disclosed in GenBank or provided by Appellants which suggest that this update resulted in a different sequence from what was available in October 6, 1995. As known in the art and indicated by Appellants in the previous Appeal Brief of 3/14/2002 (page 4, first paragraph), GenBank and

EMBL are constantly updating, annotating and/or supplementing their records. Therefore, the update of August 11, 1997 could have been a new annotation, a typographical correction, an additional author added, a new publication related to the entry, etc. As indicated in the Examiner's Answer of 5/20/2003, the National Center for Biotechnology Information (NCBI) website http://www.ncbi.nlm.nih.gov:80/entrez/sutils/girevhist.cgi, provides a Sequence Revision History tool which allows one to access the different versions, GI numbers and update dates for sequences. The existence of this tool is also disclosed in the sample GenBank record provided by Appellants in page 8 of the Appeal Brief of 3/14/2002, under "Version". As known in the art and also disclosed in the sample GenBank record provided by Appellants in the Appeal Brief of 3/14/2002 (pages 8-9, "Version" and "GI"), if there are changes made to a sequence, the version number will increase and the GI (GenInfo Identifier) number will also change. A copy of (1) the sequence corresponding to entry Z49617 as of its creation date, October 6, 1995, the sequence corresponding to entry Z49617 as of August 11, 1997, and a copy of the sequence revision history for entry Z49617 were submitted with the Examiner's Answer of 5/20/2003. Z49617 was first seen at NCBI on October 8, 1995. As shown in the revision history, there are no changes to the GI or version numbers for this entry which would indicate changes in sequence. Furthermore, a comparison of the sequences as of October 6, 1995 and August 11, 1997 do not appear to show any changes in sequence. Therefore, in the absence of any evidence which would suggest that the sequence in the instant entry was modified in 1997 or that there was a request to withhold its public disclosure until 1997, the Examiner must assume that the instant entry was first disclosed to the public on October 6, 1995.

In page 3, last paragraph, continuing on page 4, Appellants submit that SEQ ID NO: 1 and 2 are prior art since they are the inherent sequences of natural Afc1 and Rce1 transcripts. Also, Appellants submit that these sequences are prior art since they have been disclosed as part of the yeast sequencing project. Appellants argue that whether or not a portion of the yeast chromosome was sequenced prior to

the filing date of the instant application is of no consequence since the genomic sequence is an inherent aspect of the genome. Appellants submit that the invention derives from identifying two genes in isolation from the genome, and that the record does not indicate that the claimed sequences were previously isolated, characterized or in any way identified apart from the gross yeast genomic sequence. It is Appellant's contention that the entries by Rose et al. and Lye et al. were data collected as part of sequencing projects and they are no more than machine-predicted open reading frames of raw genetic sequence.

For the record, it is noted that SEQ ID NO: 1 and SEQ ID NO: 2 are not the sequences of Afc1 and Rce1 transcripts as asserted by Appellants. According to the specification, page 38, lines 1-10, SEQ ID NO: 1 provides the sequence of the Afc1 gene and SEQ ID NO: 3 provides the sequence of the Rce1 gene. It is noted that Lye et al. is irrelevant to the rejection of claims 31 and 39. The Examiner acknowledges that the entries by Rose et al. and Lye et al. are the result of yeast sequencing projects. With respect to Rose et al., the Examiner agrees that if the polynucleotide of Rose et al. would have been disclosed as just a fragment of the yeast chromosome which comprises SEQ ID NO: 1, it is less likely that one of skill in the art would have been motivated to construct an expression vector wherein the polynucleotide of Rose et al. is linked to a promoter, and transform host cells with said expression vector. However, as indicated in numerous occasions, the polynucleotide of GenBank accession No. Z49617 has not been disclosed as just a fragment of the yeast chromosome which happens to comprise the Afc1 gene. Instead, it has been disclosed as an open reading frame (ORF). As known in the art, ORFs are DNA segments which encode proteins. Therefore, if it was known that the polynucleotide of Rose et al. is an ORF, there is clear motivation to construct a vector such as the one claimed, and transform host cells with such vectors for recombinantly producing the protein. The Examiner acknowledges Appellant's contribution to the art in regard to the functional characterization of the protein of SEQ ID NO: 2 (encoded by the polynucleotide of SEQ ID NO: 1) and agrees that the ORF of Rose et al. is computer

predicted. However, as indicated in the Examiner's Answer of 5/20/2003, whether or not the ORF has been determined experimentally or predicted by a computer is irrelevant. Once an ORF is known or suspected, one would be highly motivated to construct an expression vector with the ORF linked to a promoter, and transform host cells to recombinantly produce the corresponding protein to characterize the protein and determine its biological function. In the instant case, one of ordinary skill in the art is highly motivated to characterize and determine the biological role of a yeast (*S. cerevisiae*) protein since yeast is a unicellular eukaryote widely studied in the art for identification of proteins and/or biological processes which may be found in higher eukaryotes including humans.

In page 4, second and third paragraphs, Appellants argue that the database entries used include annotations identifying the genes and functions as determined by Appellants. Therefore, it is Appellant's contention that without the information provided by them, there would be no motivation to create expression vectors. In the absence of Appellant's information, the entries are just a list of machine-construed ORFs of the yeast chromosome. According to Appellants, the Examiner identified and isolated the cited sequences only by using Appellant's disclosed sequences as probes. Without Appellant's disclosure, Appellants submit that there is no motivation to invest money and time to make the claimed expression vectors. Appellants argue that prior to their disclosure, there was no known ORF for Afc1 and that annotations in genomic databases have been updated to reflect Appellant's disclosure. Appellants conclude that there is no evidence of record, and never will, that someone other than Appellants provided motivation to isolate and express the natural sequence encoding Afc1.

It is reiterated herein that the Examiner acknowledges Appellant's contribution to the art regarding the functional characterization of the ORF disclosed by Rose et al. The Examiner also acknowledges that databases have been updated to indicate the functional characterization of the Afc1 protein disclosed by Appellants. However, the Examiner disagrees with Appellant's contention that only Appellants provided motivation to isolate and express the polynucleotide encoding the Afc1 protein or

that the Examiner used Appellant's sequences as probes. While one could argue that the motivation to construct the claimed vector and transform cells with such vector would have been even higher if the function of the Afc1 protein was known, all that is required in the obviousness analysis is showing of a motivation to make the claimed invention and a reasonable expectation of success. As indicated above, once it was known or suspected that the polynucleotide of Rose et al. was an ORF, one of skill in the art would have been highly motivated to construct the claimed expression vector and transform host cells to recombinantly produce the yeast protein for further characterization, since yeast is a unicellular eukaryote widely studied in the art for identification of proteins and/or biological processes which may be found in higher eukaryotes including humans. There is a reasonable expectation of success at making such vectors and transform host cells with such vectors in view of the fact that (1) Nozaki et al. teaches an expression vector which can be used in *E. coli* and yeast as well as the transformation of host cells with such vector, and (2) construction of expression vectors and transformation of host cells for recombinant expression of proteins is well known and widely used in the art. Thus, whether the function of the Afc1 protein encoded by the polynucleotide of Rose et al. was known or not is irrelevant to the obviousness analysis presented.

In page 5, Appellants argue that raw genomic sequence has long been subjected to computer annotation for genes, transcription factor binding sites, regulatory elements, etc. Appellants submit that computer estimations rely on simple pattern probability assessment and may be arbitrarily adjusted to nominate arbitrarily more or fewer regions. Thus, this explains why one could get different estimates as to how many genes there are in a genome, including the human genome. Applicants submit that even if the entire yeast genome sequence is prior art and even if the genome was subjected to computer reading, the Examiner should not use Applicant's disclosure of function to go back to genomic sequence and pick out one postulated sequence among innumerable false negatives and false positives.

The Examiner agrees that computer estimations in regard to annotation of genes, transcription factor binding sites, etc. may provide erroneous predictions. In addition, the Examiner, as indicated above, agrees that knowing the function of the Afc1 protein would have provided one of skill in the art even more motivation to construct the claimed vectors and transform the claimed host cells. However, it is noted that the Examiner is in no way using Appellant's functional characterization of the Afc1 protein as motivation to make the claimed invention. The fact that the yeast polynucleotide of Rose et al. was disclosed as a potential ORF would have been sufficient to highly motivate one of skill in the art to make the claimed vectors and transform host cells with such vectors in order to produce enough protein for characterization studies since yeast is a unicellular eukaryote widely studied in the art for identification of proteins and/or biological processes which may be found in higher eukaryotes including humans. Thus, even if the predicted ORF of Rose et al. was erroneous, this would have been irrelevant to the obviousness analysis, since there is clear motivation to make the claimed invention and there is a reasonable expectation of success in making the claimed invention.

Issue II: Claims 35, 37-38, 43 and 45-46 are patentable under 35 USC 103(a)

In page 5, last paragraph, Appellants argue that Lye et al. (GenBank accession No. Z49260) is dated August 11, 1997, which is more than a year after Appellant's priority date. According to Appellants, the Examiner is relying on an unpublished submission date, which is improper according to MPEP 2128. It is Appellant's contention that the Action provides no evidence that the prior art sequence was published any time prior to August 11, 1997.

The Examiner cannot determine which unpublished submission date is being referred to by Appellants. The record clearly shows a PTO 892 submitted to Appellants on 3/27/2001 along with a Final Action. In this PTO 892, the previous Examiner of record cited Lye et al. and indicated a date for this entry, May 16, 1995. In addition, the record shows the submission to Appellants of copies of the Lye

et al. reference by the previous Examiner of record, which is a printout of the corresponding GenBank entry Z49260 where the date is placed on the line immediately after the accession number on the right hand side. Also, the present Examiner of record submitted with the Examiner's Answer of 5/20/2003 a copy of an e-mail communication with a representative from EMBL indicating that the creation date of the Z49260 entry is the date of public availability. The existence of this e-mail communication was made known to Appellants in the Advisory Action of 2/21/2002 and was submitted to Appellants with the Examiner's Answer of 5/20/2003 for record completeness. In that e-mail communication, it is clearly stated that the creation date of entry Z49260 is May 16, 1995, under DT. Therefore, contrary to Appellant's assertion, (1) Appellants have been provided with a copy of the cited reference where the creation date was printed, and (2) sufficient evidence has been presented to show that the sequence of Lye et al. was first disclosed on May 16, 1995 and not August 11, 1997 as asserted by Appellants.

The Examiner acknowledges that entry Z49260 was updated in August 11, 1997. However there is no evidence in the record as disclosed in GenBank/EMBL or provided by Appellants which suggest that this update resulted in a different sequence from what was available in May 16, 1995. As known in the art and indicated by Appellants in the previous Appeal Brief of 3/14/2002 (page 4, first paragraph), GenBank and EMBL are constantly updating, annotating and/or supplementing their records, therefore the update of August 11, 1997 could have been a new annotation, a typographical correction, an additional author added, a reference to a new publication related to that entry, etc. As indicated in the Examiner's Answer of 5/20/2003, the National Center for Biotechnology Information (NCBI) website http://www.ncbi.nlm.nih.gov:80/entrez/sutils/girevhist.cgi, provides a Sequence Revision History tool which allows one to access the different versions, GI numbers and update dates for sequences. The existence of this tool is also disclosed in the sample GenBank record provided by Appellants in page 8 of the Appeal Brief filed on 3/14/2002, under "Version". A copy of (1) the sequence corresponding to entry Z49260 as of its creation date, May 16, 1995, the sequence corresponding to entry Z49260 as of

August 11, 1997, and a copy of the sequence revision history for entry Z49260 were submitted with the Examiner's Answer of 5/20/2003. Z49260 was first seen at NCBI on May 19, 1995. As shown in the revision history, there are no changes to the GI or version numbers for this entry which would indicate changes in sequence. Appellants have presented no evidence which would suggest that the polynucleotide disclosed by Lye et al. was withheld from public disclosure after its creation date or that it was updated or amended to the extent that its sequence is different from what it was when it was created in May 16, 1995. In the absence of any evidence which would suggest that the sequence in the instant entry was modified in 1997 or that there was a request to withhold its public disclosure until 1997, the Examiner must assume that the instant entry was first disclosed to the public on May 16, 1995. Therefore, in view of the information provided by EMBL, as evidenced by the e-mail communication provided, and the information disclosed by NCBI, one would reasonably conclude that the creation date of entry Z49260 is the date of public availability and that no sequence changes have been made to such entry. As such, the polynucleotide of Lye et al. is considered valid prior art.

In page 6, Appellants argue that SEQ ID NO: 1-2 are in the prior art since they are the inherent sequences of natural Afc1 and Rce1 transcripts. Also, Appellants submit that these sequences are prior art since they have been disclosed as part of the yeast sequencing project. Appellants argue that Lye discloses computer predictions of thousands of possible CDS regions. Appellants refer to the Comment section of the GenBank entry where the methodology used in determining the CDS is discussed. According to Appellants, Lye does not disclose any gene or gene product but the results of a first run effort to sequence the entire XIII *S. cerevisiae* chromosome. It is Appellant's contention that Lye discloses no more than the inherent property of that chromosome, i.e. its sequence, and that the Examiner uses Appellant's disclosure to provide motivation for the claimed invention. Appellants submit that in the absence of function, there is no motivation to select out one of the thousands of yeast ORFs of unknown

function, isolate what may or may not be a coding sequence, join it to a promoter in an expression vector, as recited in the claims.

For the record, it is noted that SEQ ID NO: 1 and SEQ ID NO: 2 are not the sequences of Afc1 and Rce1 transcripts as asserted by Appellants. According to the specification, page 38, lines 1-10, SEQ ID NO: 1 provides the sequence of the Afc1 gene and SEQ ID NO: 3 provides the sequence of the Rce1 gene. The Examiner agrees that if the polynucleotide of Lye et al. would have been disclosed as just a fragment of the yeast chromosome which comprises SEQ ID NO: 3, it is less likely that one of skill in the art would have been motivated to construct an expression vector wherein the polynucleotide of Lye et al. is linked to a promoter, and transform host cells with said expression vector. However, as indicated in many occasions, contrary to Appellant's assertions, the polynucleotide of GenBank accession No. Z49260 has not been disclosed as just a fragment of the yeast chromosome which happens to comprise the Rce1 gene. Instead, it has been disclosed as an open reading frame (ORF). As known in the art, ORFs are DNA segments which encode proteins. Therefore, if it was known that the polynucleotide of Lye et al. is an ORF, there is motivation to construct a vector such as the one claimed, and transform host cells with such vectors for recombinantly producing the protein.

The Examiner agrees that the ORF of Lye et al. is computer predicted and that in some cases these computer predictions may be erroneous. However, as indicated in the Examiner's Answer of 5/20/2003, whether or not the ORF has been determined experimentally or predicted by a computer is irrelevant to the obviousness analysis since there is a clear motivation to make the claimed invention and there is a reasonable expectation of success in making the claimed invention. Once an ORF is known or suspected, one would be highly motivated to construct an expression vector with the ORF linked to a promoter, and transform host cells to recombinantly produce the corresponding protein to characterize the protein and determine its biological function. In the instant case, one of ordinary skill in the art is highly motivated to characterize and determine the biological role of a yeast (*S. cerevisiae*) protein since yeast is

a unicellular eukaryote widely studied in the art for identification of proteins and/or biological processes which may be found in higher eukaryotes including humans. Furthermore, there is a reasonable expectation of success at making such vectors and transform host cells with such vectors in view of the fact that (1) Nozaki et al. teaches an expression vector which can be used in *E. coli* and yeast as well as the transformation of host cells with such vector, and (2) construction of expression vectors and transformation of host cells for recombinant expression of proteins is well known and widely used in the art.

The Examiner disagrees with Appellant's contentions that the Examiner uses Appellant's disclosure to provide motivation for the claimed invention, or that in the absence of function, there is no motivation to select out one of the thousands of yeast ORFs of unknown function, and insert such ORF in an expression vector, as recited in the claims. The Examiner is in no way using Appellant's disclosed function for the Rce1 protein as motivation to make the claimed invention. The fact that the yeast polynucleotide of Lye et al. was disclosed as a potential ORF would have been sufficient to highly motivate one of skill in the art to make the claimed vectors and transform host cells with such vectors in order to produce enough protein for characterization studies. It is reiterated herein that yeast is a unicellular eukaryote widely studied in the art for identification of proteins and/or biological processes which may be found in higher eukaryotes including humans.

While one could argue that the motivation to construct the claimed vector and transform cells with such vector would have been even higher if the function of the Rce1 protein was known, all that is required in the obviousness analysis is showing of a motivation to make the claimed invention and a reasonable expectation of success. As indicated above, once it was known or suspected that the polynucleotide of Lye et al. was an ORF, one of skill in the art would have been highly motivated to construct the claimed expression vector and transform host cells to recombinantly produce the yeast protein. Also, as previously indicated, there is a reasonable expectation of success at making the claimed

invention in view of the teachings of Nozaki et al. and what is well known in the art. Thus, whether the function of the Rce1 protein encoded by the polynucleotide of Lye et al. was known or not is irrelevant to the obviousness analysis presented.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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DR
February 16, 2005

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